K021877

AUG 0 7 2002

510(k) SUMMARY

MDA® D-Dimer

This summary of safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and the final rule under 21 CFR 807.92 published December 14, 1994.

(a) (1) **The submitter's name, address, telephone number, a contact person, and the date the summary was prepared;**

Submitter's Name:	bioMérieux Inc.
Submitter's Address:	100 Rodolphe Street Durham, North Carolina 27712, USA
Submitter's Telephone:	(919) 620-2373
Submitter's Fax:	(919) 620-2548
Submitter's Contact:	Ron Sanyal
Date 510(k) Summary Prepared:	June 6, 2002

(a) (2) **The name of the device, including the trade or proprietary name if applicable, the common or usual name, and the classification name, if known;**

Trade/Proprietary Name:	MDA® D-Dimer
Common/ Usual Name:	Fibrin Degradation Product
Classification Name:	Fibrin Degradation Product

(a) (3) **An identification of the legally marketed device to which the submitter claims substantial equivalence.**

Device Equivalent to: 1. MDA® D-Dimer (K000492)

(a) (4) **A description of the device(System)**

bioMérieux Inc. **MDA® D-Dimer** is a homogeneous latex particle based immunoassay for the quantitative determination of cross-linked fibrin degradation products containing the D-dimer domain in citrated human plasma.

D-dimer containing fibrin degradation products (FbDP) fragments are released when cross-linked fibrin is degraded by plasmin. Cross-linked fibrin is formed when fibrionogen is cleaved by thrombin to form fibrin monomers, which then spontaneously polymerize and are cross-linked by Factor XIIIa. Thrombin is required to cleave fibrinogen as well as to activate Factor XIII. Plasmin formation is triggered when a fibrin clot is formed. Plasmin degrades some of the cross-linked fibrin and the resulting level of D-dimer is, therefore, an indirect measure of thrombin generation and subsequent clot formation.

D-dimer is elevated in disseminated intravascular coagulation (DIC), deep vein thrombosis (DVT), pulmonary embolism (PE), sickle cell crisis, pre-eclampsia, some cause of unstable angina, myocardial infarction, some cancers, and following major surgery or trauma.

MDA® D-Dimer is a quantitative homogeneous-phase immunoassay using latex microparticles to photo-optically detect binding of specific monoclonal antibody to D-dimer. These latex particles aggregate in the presence of fibrin derivatives containing the D-dimer domain. The rate of latex microparticle aggregation is proportional to the concentration of D-dimer in the sample. D-dimer concentration may be interpolated from a reference curve.

(a) (5) **A statement of the intended use of the device.**

MDA D-Dimer is a homogeneous latex particle based immunoassay for the quantitative determination of cross-linked fibrin degradation products containing the D-dimer domain in citrated human plasma. MDA D-Dimer is an assay for use in conjunction with a clinical Pre-test Probability Assessment (PTP) model in excluding deep vein thrombosis (DVT) in outpatients suspected of a first episode of DVT. MDA D-Dimer can also be used as an aid in the assessment and evaluation of patients suspected of pulmonary embolism (PE). The assay is designed for use on the MDA automated coagulation analyzers.

(a) (6) **A summary of the technological characteristics of the new device in comparision to those of the predicate device.**

The technological characteristics of the device **MDA® D-Dimer** in comparison to those of the 510(k) cleared device **MDA® D-Dimer assay (K000492)** are given in the table 1 below.

Table 1

Category	MDA® D-Dimer assay (K000942)	MDA® D-Dimer
Medical Device	Yes	Yes
Intended Use	**MDA® D-Dimer** is a homogeneous latex particle based immunoassay for the quantitative determination of cross-linked fibrin degradation products containing the D-dimer domain in citrated human plasma. MDA D-Dimer can be used to aid in the assessment and evaluation of patients suspected of venous thromboembolism (VTE), which is comprised of deep vein thrombosis (DVT) and pulmonary embolism (PE). The assay is designed for use on the MDA automated coagulation analyzers.	**MDA® D-Dimer** is a homogeneous latex particle based immunoassay for the quantitative determination of cross-linked fibrin degradation products containing the D-dimer domain in citrated human plasma. MDA D-Dimer can be used to aid in the assessment and evaluation of patients suspected of venous thromboembolism (VTE), which is comprised of deep vein thrombosis (DVT) and pulmonary embolism (PE). The assay is designed for use on the MDA automated coagulation analyzers.
Regulatory Class	Class II	Class II
Product Code	DAP	DAP
Classification Panel	Hematology	Hematology
C.F.R. Section	21 CFR 864.7320	21 CFR 864.7320
Presentation	Automated Latex Immunoassay	Automated Latex Immunoassay
Format	Quantitative	Quantitative
Instrument	MDA® automated coagulation analyzers	MDA® automated coagulation analyzers
Reagents	Same	Same
Principle of the procedure	Same	Same
Quality Control	Same	Same
Test Procedure	Same	Same
Reference Curve Range	0-4.0 µg FEU/ml	0-4.0 µg FEU/ml

(b) (1) **A brief discussion of the nonclinical tests submitted, reference, or relied on in the premarket notification submission for a determination of substantial equivalency.**

Not Applicable

(b)(2) **A brief discussion of the clinical tests submitted, reference, or relied on in the premarket notification submission for a determination of substantial equivalency.**

Comparison Data:

Performance Characteristics

Specificity

MDA D-Dimer Latex Reagent aggregates in the presence of cross-linked fibrin degradation products D-dimer and D-dimer E.

Accuracy

Results from **MDA D-Dimer** reagents obtained on an MDA were compared with a commercially available assay (Fibrinostika® FbDP EIA)for detection of crosslinked and non–crosslinked fibrin degradation product containing the D-dimer. Specimens were tested in duplicate according to NCCLS Approved Guideline EP9-A.[29] The following results for slope, intercept and correlation were observed for linear least squares regression comparing **MDA D-Dimer** (y-axis) and the reference method (x-axis):

Reference Method	n	Slope	Intercept	r
Fibrinostika® FbDP EIA	175	1.005	0.293	0.91

Precision

Total precision and within-run precision for the **MDA D-Dimer** assay were determined in accordance with NCCLS Tentative Guideline EP5-T2.[30] Controls were tested in duplicate on an MDA instrument twice daily. Data were collected for 20 days, with a minimum of 40 runs and 80 measurements at each control level. The following precision was observed:

Sample	Mean (µg FEU/ml)	SD (within-run) (µg FEU/ml)	CV (within-run) (%)	SD(total) (µg FEU/ml)	CV(total) (%)
Positive Control	1.51	0.06	3.83	0.10	6.67
MDA Verify 1 (Normal Control)	0.28	0.02	6.97	0.04	12.65

Clinical Performance

A multi-center, prospective cohort study was designed to validate the diagnostic utility of the MDA D-Dimer assay to exclude a diagnosis of deep vein thrombosis (DVT).[9] Consecutive eligible outpatients (n = 556) with a first suspected DVT episode were evaluated at three hospitals. Using a previously validated standardized clinical model [9] to estimate the probability of DVT, patients were classified as having a high, moderate, or low pre-test- probability – (PTP) of DVT, and had an MDA D-Dimer test performed on presentation.

The D-Dimer assay was performed without knowledge of the PTP assessment results. A clinical cut off value of 0.50 µg FEU/ml previously validated in an accuracy study[9] was used. A D-Dimer result of ≥0.50 µg FEU/ml was considered positive, and a result of <0.50 µg FEU/ml was considered negative.

The overall prevalence of DVT in the total population studied was 10.1% (56/556). The sensitivity, specificity and negative predictive value of the MDA D-Dimer assay for a clinical cut off of 0.50 µg FEU/ml are summarized below with the corresponding 95% confidence interval (CI).

Patients	N	% Clinical Sensitivity (95% CI)	% Clinical Specificity (95% CI)	% Negative Predictive Value (95% CI)
Suspected DVT	556	98.2 (90-100 CI)	60.4 (56-65 CI)	99.7 (98-100 CI)

This study was designed as a management clinical trial and patients were grouped according to PTP. Those patients having a negative MDA D-Dimer test result and a low or moderate PTP of DVT underwent no further diagnostic testing and were followed up for 3 months for development of DVT. Patients with a positive MDA D-Dimer and/or high PTP underwent serial compression ultrasound (CUS).

The results of this study suggest that a negative MDA D-Dimer test result in conjunction with Wells clinical Pre-test probability Assesment (PTP) model excludes clinically significant DVT in out patients with a first suspected episode. In addition, this test provides a rapid, automated diagnostic tool and eliminates the need to expose patients to invasive procedures or unnecessary treatment.

(b) (3) **The conclusion drawn from the nonclinical and clinical tests that demonstrate that the device is as safe, as effective, and performed as well or better than the legally marketed device identified in (a) (3).**

In conclusion, the MDA® D-Dimer has successfully met all aspects of non-clinical and clinical testing and have demonstrated that the device is safe and effective and has performed well and is substantially equivalent to the legally marketed device **MDA® D-Dimer assay (K000492).**

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

AUG 0 7 2002

Mr. Ron Sanyal, M. Pharm, CQE, RAC
Acting Head of Regulatory Affairs
BioMerieux, Inc.
100 Rodolphe Street
Durham, North Carolina 27712

Re: k021877
Trade/Device Name: MDA® D-Dimer
Regulation Number: 21 CFR § 864.7320
Regulation Name: Fibrin Degradation Product
Regulatory Class: II
Product Code: GHH
Dated: June 6, 2002
Received: June 7, 2002

Dear Mr. Sanyal:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) NUMBER (IF KNOWN): K021877

DEVICE NAME: MDA® D-Dimer

5.0 INDICATIONS FOR USE:

MDA® D-Dimer is a homogeneous latex particle based immunoassay for the quantitative determination of cross-linked fibrin degradation products containing the D-dimer domain in citrated human plasma. MDA D-Dimer is an assay for use in conjunction with a clinical Pre-test Probability Assessment (PTP) model in excluding deep vein thrombosis (DVT) in outpatients suspected of a first episode of DVT. MDA D-Dimer can also be used as an aid in the assessment and evaluation of patients suspected of pulmonary embolism (PE). The assay is designed for use on the MDA automated coagulation analyzers.

Josephine Bautista

(Division Sign-Off)
Division of Clinical Laboratory Devices

510(k) Number K021877

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED.)

Concurrence of CDRH, Office of Device Evaluation (ODE)

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Prescription Use ____ (Per 21 CFR 801.109)

OR

Over-The-Counter-Use____ (Optional Format 1-2-96)